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Executive Director
Office for Human Research Protections
Office of Public Health and Science, OS
6100 Executive Boulevard, Room 3B01 (MSC 7507)
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Dear Ms. Gottfried:

The Johns Hopkins University School of Medicine wishes to comment on OHRP's Draft Interim Guidance titled "Financial Relationships in Clinical Research: Issues for Institutions, Clinical Investigators, and IRBs to Consider When Dealing with Issues of Financial Interests and Human Subject Protection." We recognize and applaud OHRP's goal of bringing issues concerning conflict of interest to the attention of institutions and investigators. However, we are concerned that the guidance overlaps with many areas of current regulation, including existing PHS and FDA regulations regarding disclosure and management of financial interests and conflicts of interest.

Section 1.1 of the guidance acknowledges that while conflict of interest policies are not uniform across institutions, as a result of existing regulations many institutions have established committees to review and manage conflicts of interest in research, including human subjects research. The School of Medicine has had a conflict of interest policy in place since 1992. In connection with that policy, the School follows well-developed procedures to review and manage relevant financial interests on the part of investigators and the institution. Based on our years of experience, we believe that while close coordination between the IRB and the body charged with reviewing and managing conflict of interest is essential, the latter function should be carried out independently of the IRB. Requiring IRBs to manage conflict of interest issues will cause confusion among IRB members, investigators, and Institutions; and increase the Institutional cost and burden to interpret and comply with overlapping requirements from several governmental agencies.

We would like to bring to your attention several sections of the guidance which are of specific concern.

Section 1.2 suggests that investigators should supply to the institutional official, who in turn should supply to the IRB, copies of disclosures that are provided to sponsors. It is not clear how this requirement would serve to protect human subjects participating in research studies. We wish to point out that sponsors are required to submit such information to the FDA at the time a marketing permit is submitted to FDA. Many studies never reach this stage. Therefore, a) such disclosure may come too late in the process to enhance protection of human subjects, and b) such disclosure may be duplicative of institutions' existing internal disclosure and conflict of interest management requirements, typically established to comply both with PHS and institutional policies on conflict of interest. The merit of adding this requirement should be further enunciated by OHRP.

Section 1.4 indicates that institutions should collect and review conflict of interest information regarding IRB members and staff. This requirement must now be met by institutions that have assured PHS that they are in accord with current regulations. IRB chairs, affiliated members, and staff who have financial conflicts of interest are covered by current PHS requirements for disclosure. As stated in the guidance, the requirement to disclose would be extended to the unaffiliated members of the IRB. The new requirement would be duplicative of existing regulations and the intent of the guidance with regard to the suggestions in 1.4 should be clarified.

Section 1.6 identifies concerns regarding institutional conflicts of interest. It is not clear from the guidance who or what mechanism should be employed to "carefully consider whether a clinical trial to evaluate safety and efficacy should be performed at that site, and if it should, what special protections would be needed." Although the guidance is careful to indicate that IRBs should not be further burdened by implementation of these suggestions, we would observe that development of "special protections" has routinely fallen to IRBs. This section also refers to "special safeguards to maximally protect the scientific integrity of the study and research participants," without providing guidance on who should develop the safeguards. We would suggest that, rather than burdening IRBs with the determination and management of potential institutional conflicts of interest, this matter should be addressed through the institution's overall conflict of interest review and management process.

Section 1.8 would involve the IRB in a process that is now covered by institutional conflict of interest committees and by grants administration offices. IRBs are not routinely involved in the negotiation of budgets for clinical studies with commercial sponsors or in intellectual property negotiations. Although Section 1.8 indicates IRB Chairs or staff should receive financial conflict of interest information, it does not demonstrate how such information will be used to enhance protection of human subjects. This provision would increase the paperwork burden on the IRB and possibly compel it to duplicate the activity of the institutional conflict of interest committee. It also should be noted that this section appears to cover an extremely broad spectrum of "relationships

that the institution has with the commercial sponsor of a study...." For example, "any equity interest in the commercial sponsor" could mean stock held in the institution's endowment, a holding which is completely unrelated to a specific human subjects protocol.

Section 4 would extend IRB burden significantly beyond that specified in current regulations. The added requirement that "The IRB should consider all categories in the PHS regulations on Financial Conflict of Interest and the FDA Financial Disclosure Regulations..." would duplicate the review process which already is required and is conducted by the institutional conflict of interest committee or appropriate official. Although section 4.3 indicates that "the IRB might wish to consider the answer to the following questions in its deliberations," past experience has shown that OHRP takes such "guidance" statements as requirements rather than points to consider. We urge OHRP to allow institutions flexibility in determining the appropriate infrastructure needed to perform conflict of interest review and management, IRB review, and review of proposed budget arrangements with sponsors, rather than including in the guidance specific additional review requirements for IRBs themselves.

Section 5 contains three suggestions for inclusion of funding source and financial conflict of interest information in consent documents. There is concern on the part of many IRBs that consent forms already are too long and detailed for participants to understand the research project that is being presented. Many institutions are concerned that inclusion of financial disclosures would add to the length and complexity of consent forms. IRBs, Conflict of Interest Committees, and/or institutions should have the option of including financial disclosures in the consent document itself or developing a mechanism of providing this information in some other way. If OHRP believes strongly that the information must be contained in a consent form, we believe that the human subjects regulations on informed consent should be amended to include a new required element, rather than suggesting this as part of a "guidance" document, which is then held to be "regulation."

We are pleased that OHRP has provided an opportunity to comment on the proposed guidance document and we look forward to further discussion on issues concerning financial conflict of interest in human subjects research.

Sincerely yours,

Chi Van Dang, M.D., Ph.D.
Vice Dean for Research

CVD:bls
Cc: General Counsel's Office - JHU and JHHS
Dr. Gary Briefel - Chair, JHBMC IRB
Dr. Curt Civin - Chair, Committee on Conflict of Interest
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